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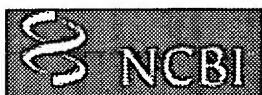
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<i>DB=USPT; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L36	5789230.pn. and papilloma virus	1
<input type="checkbox"/>	L35	5789230.pn. and papillomavirus	0
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<input type="checkbox"/>	L33	5855891.pn.	1
<i>DB=PGPB; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L32	deleted "L1" epitope	0
<input type="checkbox"/>	L31	deleted "L1" antigne	0
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<input type="checkbox"/>	L28	empty virus like particles	4
<input type="checkbox"/>	L27	papillomavirus and empty virus like particles	0
<input type="checkbox"/>	L26	empty virus like particles and papillomavirus	0
<input type="checkbox"/>	L25	L2 and papillomavirus	0
<i>DB=EPAB; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L24	WO-9746693-A1.did.	1
<input type="checkbox"/>	L23	WO-9746693-A1.did.	1
<i>DB=USOC; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L22	major capsid protein and human papilloma virus modified and nonimmunogenic	0
<i>DB=EPAB; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L21	major capsid protein and human papilloma virus modified and nonimmunogenic	0
<i>DB=JPAB; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L20	major capsid protein and human papilloma virus modified and nonimmunogenic	0
<i>DB=DWPI; PLUR=YES; OP=ADJ</i>			
<input type="checkbox"/>	L19	major capsid protein and human papilloma virus modified and nonimmunogenic	1
<input type="checkbox"/>	L18	major capsid protein of human papilloma virus modified to be nonimmunogenic	0
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		<i>DB=EPAB; PLUR=YES; OP=ADJ</i>	
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		<i>DB=DWPI; PLUR=YES; OP=ADJ</i>	
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<input type="checkbox"/>	L11	Bloch.in. virus like	0
<input type="checkbox"/>	L10	Bloch.in. gene therapy	0
<input type="checkbox"/>	L9	Bloch.in. VLP	0
<input type="checkbox"/>	L8	Bloch.in.	496
<input type="checkbox"/>	L7	Bloch.in. and papillomavirus	0
		<i>DB=USPT; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L6	Bloch.in. and papillomavirus	1
<input type="checkbox"/>	L5	Bloch.in. and papilomavirus	0
<input type="checkbox"/>	L4	L2 and papillomavirus	1
<input type="checkbox"/>	L3	L2 and papillomairus	0
<input type="checkbox"/>	L2	empty virus like particles	8
<input type="checkbox"/>	L1	papillomavirus and virus like particles	137

END OF SEARCH HISTORY



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Items 1-20 of 131

Page 1 of 7 Next

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- 1: [Carter JJ, Wipf GC, Benki SF, Christensen ND, Galloway DA.](#) Related Articles, Links  
 Identification of a human papillomavirus type 16-specific epitope on the C-terminal arm of the major capsid protein L1.  
*J Virol.* 2003 Nov;77(21):11625-32.  
PMID: 14557648 [PubMed - indexed for MEDLINE]
- 2: [Christensen ND, Cladel NM, Reed CA, Budgeon LR, Embers ME, Skulsky DM, McClements WL, Ludmerer SW, Jansen KU.](#) Related Articles, Links  
 Hybrid papillomavirus L1 molecules assemble into virus-like particles that reconstitute conformational epitopes and induce neutralizing antibodies to distinct HPV types.  
*Virology.* 2001 Dec 20;291(2):324-34.  
PMID: 11878901 [PubMed - indexed for MEDLINE]
- 3: [White WI, Wilson SD, Palmer-Hill FJ, Woods RM, Ghim SJ, Hewitt LA, Goldman DM, Burke SJ, Jenson AB, Koenig S, Suzich JA.](#) Related Articles, Links  
 Characterization of a major neutralizing epitope on human papillomavirus type 16 L1.  
*J Virol.* 1999 Jun;73(6):4882-9.  
PMID: 10233949 [PubMed - indexed for MEDLINE]
- 4: [Combita AL, Touze A, Bousarghin L, Christensen ND, Coursaget P.](#) Related Articles, Links  
 Identification of two cross-neutralizing linear epitopes within the L1 major capsid protein of human papillomaviruses.  
*J Virol.* 2002 Jul;76(13):6480-6.  
PMID: 12050360 [PubMed - indexed for MEDLINE]
- 5: [Varsani A, Williamson AL, de Villiers D, Becker I, Christensen ND, Rybicki EP.](#) Related Articles, Links  
 Chimeric human papillomavirus type 16 (HPV-16) L1 particles presenting the common neutralizing epitope for the L2 minor capsid protein of HPV-6 and HPV-16.  
*J Virol.* 2003 Aug;77(15):8386-93.  
PMID: 12857908 [PubMed - indexed for MEDLINE]
- 6: [Christensen ND, Dillner J, Eklund C, Carter JJ, Wipf GC, Reed CA, Cladel NM, Galloway DA.](#) Related Articles, Links  
 Surface conformational and linear epitopes on HPV-16 and HPV-18 L1 virus-like particles as defined by monoclonal antibodies.  
*Virology.* 1996 Sep 1;223(1):174-84.  
PMID: 8806551 [PubMed - indexed for MEDLINE]

- 7: [Wang XM, Cook JC, Lee JC, Jansen KU, Christensen ND, Ludmerer SW, McClements WL.](#) [Related Articles](#), [Links](#)
-  Human papillomavirus type 6 virus-like particles present overlapping yet distinct conformational epitopes.  
J Gen Virol. 2003 Jun;84(Pt 6):1493-7.  
PMID: 12771418 [PubMed - indexed for MEDLINE]
- 8: [McClements WL, Wang XM, Ling JC, Skulsky DM, Christensen ND, Jansen KU, Ludmerer SW.](#) [Related Articles](#), [Links](#)
-  A novel human papillomavirus type 6 neutralizing domain comprising two discrete regions of the major capsid protein L1.  
Virology. 2001 Oct 25;289(2):262-8.  
PMID: 11689049 [PubMed - indexed for MEDLINE]
- 9: [Sadeyen JR, Tourne S, Shkreli M, Sizaret PY, Coursaget P.](#) [Related Articles](#), [Links](#)
-  Insertion of a foreign sequence on capsid surface loops of human papillomavirus type 16 virus-like particles reduces their capacity to induce neutralizing antibodies and delineates a conformational neutralizing epitope.  
Virology. 2003 Apr 25;309(1):32-40.  
PMID: 12726724 [PubMed - indexed for MEDLINE]
- 10: [Christensen ND, Reed CA, Cladel NM, Hall K, Leiserowitz GS.](#) [Related Articles](#), [Links](#)
-  Monoclonal antibodies to HPV-6 L1 virus-like particles identify conformational and linear neutralizing epitopes on HPV-11 in addition to type-specific epitopes on HPV-6.  
Virology. 1996 Oct 15;224(2):477-86.  
PMID: 8874508 [PubMed - indexed for MEDLINE]
- 11: [Volpers C, Sapp M, Snijders PJ, Walboomers JM, Streeck RE.](#) [Related Articles](#), [Links](#)
-  Conformational and linear epitopes on virus-like particles of human papillomavirus type 33 identified by monoclonal antibodies to the minor capsid protein L2.  
J Gen Virol. 1995 Nov;76 ( Pt 11):2661-7.  
PMID: 7595373 [PubMed - indexed for MEDLINE]
- 12: [Wang X, Wang Z, Christensen ND, Dillner J.](#) [Related Articles](#), [Links](#)
-  Mapping of human serum-reactive epitopes in virus-like particles of human papillomavirus types 16 and 11.  
Virology. 2003 Jun 20;311(1):213-21.  
PMID: 12832218 [PubMed - indexed for MEDLINE]
- 13: [Kawana K, Matsumoto K, Yoshikawa H, Taketani Y, Kawana T, Yoshiike K, Kanda T.](#) [Related Articles](#), [Links](#)
-  A surface immunodeterminant of human papillomavirus type 16 minor capsid protein L2.  
Virology. 1998 Jun 5;245(2):353-9.  
PMID: 9636375 [PubMed - indexed for MEDLINE]
- 14: [Touze A, El Mehdaoui S, Sizaret PY, Mougin C, Munoz N, Coursaget P.](#) [Related Articles](#), [Links](#)
-  The L1 major capsid protein of human papillomavirus type 16 variants affects yield of virus-like particles produced in an insect cell expression system.  
J Clin Microbiol. 1998 Jul;36(7):2046-51.

PMID: 9650960 [PubMed - indexed for MEDLINE]

- 15: [Cason J, Patel D, Naylor J, Lunney D, Shepherd PS, Best JM, McCance DJ.](#) [Related Articles](#), [Links](#)

 Identification of immunogenic regions of the major coat protein of human papillomavirus type 16 that contain type-restricted epitopes.  
J Gen Virol. 1989 Nov;70 ( Pt 11):2973-87.  
PMID: 2479716 [PubMed - indexed for MEDLINE]

- 16: [Chen Y, Ghim SJ, Jenson AB, Schlegel R.](#) [Related Articles](#), [Links](#)

 Mutant canine oral papillomavirus L1 capsid proteins which form virus-like particles but lack native conformational epitopes.  
J Gen Virol. 1998 Sep;79 ( Pt 9):2137-46.  
PMID: 9747722 [PubMed - indexed for MEDLINE]

- 17: [Christensen ND, Kirnbauer R, Schiller JT, Ghim SJ, Schlegel R, Jenson AB, Kreider JW.](#) [Related Articles](#), [Links](#)

 Human papillomavirus types 6 and 11 have antigenically distinct strongly immunogenic conformationally dependent neutralizing epitopes.  
Virology. 1994 Nov 15;205(1):329-35.  
PMID: 7526536 [PubMed - indexed for MEDLINE]

- 18: [Kulski JK, Sadleir JW, Kelsall SR, Cicchini MS, Shellam G, Peng SW, Qi YM, Galloway DA, Zhou J, Frazer IH.](#) [Related Articles](#), [Links](#)

 Type specific and genotype cross reactive B epitopes of the L1 protein of HPV16 defined by a panel of monoclonal antibodies.  
Virology. 1998 Apr 10;243(2):275-82.  
PMID: 9568027 [PubMed - indexed for MEDLINE]

- 19: [Ludmerer SW, Benincasa D, Mark GE 3rd, Christensen ND.](#) [Related Articles](#), [Links](#)

 A neutralizing epitope of human papillomavirus type 11 is principally described by a continuous set of residues which overlap a distinct linear, surface-exposed epitope.  
J Virol. 1997 May;71(5):3834-9.  
PMID: 9094659 [PubMed - indexed for MEDLINE]

- 20: [Roden RB, Armstrong A, Haderer P, Christensen ND, Hubbert NL, Lowy DR, Schiller JT, Kirnbauer R.](#) [Related Articles](#), [Links](#)

 Characterization of a human papillomavirus type 16 variant-dependent neutralizing epitope.  
J Virol. 1997 Aug;71(8):6247-52.  
PMID: 9223527 [PubMed - indexed for MEDLINE]

Items 1-20 of 131

Page  of 7 Next

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(FILE 'HOME' ENTERED AT 13:03:11 ON 12 AUG 2004)

FILE 'MEDLINE' ENTERED AT 13:03:19 ON 12 AUG 2004

L1 14951 S PAPILLOMAVIRUS  
L2 159 S VLP AND L1  
L3 2173 S VIRUS LIKE PARTICLES  
L4 321 S L3 AND L1  
L5 53 S CARRIER AND L3  
L6 46 S EMPTY AND L3  
L7 26 S GENE THERAPY AND L3

L7 ANSWER 1 OF 26 MEDLINE on STN  
AN 2004135757 MEDLINE  
DN PubMed ID: 14973544  
TI DNA vaccine-encapsulated **virus-like particles**  
derived from an orally transmissible virus stimulate mucosal and systemic  
immune responses by oral administration.  
AU Takamura S; Niikura M; Li T-C; Takeda N; Kusagawa S; Takebe Y; Miyamura T;  
Yasutomi Y  
CS Department of Bioregulation, Mie University School of Medicine, Tsu, Mie,  
Japan.  
SO Gene therapy, (2004 Apr) 11 (7) 628-35.  
Journal code: 9421525. ISSN: 0969-7128.  
CY England: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200407  
ED Entered STN: 20040319  
Last Updated on STN: 20040722  
Entered Medline: 20040721  
AB Delivery of foreign genes to the digestive tract mucosa by oral  
administration of nonreplicating gene transfer vectors would be a very  
useful method for vaccination and **gene therapy**.  
However, there have been few reports on suitable vectors. In the present  
study, we found that plasmid DNA can be packaged in vitro into a  
virus-like particle (VLP) composed of open reading frame 2 of hepatitis E  
virus, which is an orally transmissible virus, and that these VLPs can  
deliver this foreign DNA to the intestinal mucosa in vivo. The delivery  
of plasmid DNA to the mucosa of the small intestine was confirmed by the  
results of immunohistochemical analyses using an expression plasmid  
encoding human immunodeficiency virus env (HIV env) gp120. After oral  
administration of VLPs loaded with HIV env cDNA, significant levels of  
specific IgG and IgA to HIV env in fecal extracts and sera were found.  
Moreover, mice used in this study exhibited cytotoxic T-lymphocyte  
responses specific to HIV env in the spleen, Payer's patches and  
mesenteric lymph nodes. These findings suggest that VLPs derived from  
orally transmissible viruses can be used as vectors for delivery of genes  
to mucosal tissue by oral administration for the purpose of DNA  
vaccination and **gene therapy**.  
CT Check Tags: Female; Support, Non-U.S. Gov't  
\*AIDS Vaccines: GE, genetics  
Administration, Oral  
Animals  
Cell Line  
\*Gene Therapy: MT, methods  
\*Genetic Vectors: AD, administration & dosage  
\*Hepatitis E virus: GE, genetics  
Immunity, Mucosal  
\*Intestinal Mucosa: IM, immunology  
Mice  
Mice, Inbred BALB C  
\*Open Reading Frames  
T-Lymphocytes, Cytotoxic: IM, immunology  
CN 0 (AIDS Vaccines); 0 (Genetic Vectors)  
  
L7 ANSWER 2 OF 26 MEDLINE on STN  
AN 2003592752 MEDLINE  
DN PubMed ID: 14645925  
TI Murine pneumotropic virus VP1 **virus-like**  
**particles** (VLPs) bind to several cell types independent of sialic  
acid residues and do not serologically cross react with murine

polyomavirus VP1 VLPs.

AU Tegerstedt K; Andreasson K; Vlastos A; Hedlund K O; Dalianis T; Ramqvist T

CS Department of Oncology-Pathology, Karolinska Institute, Cancer Center

Karolinska R8 : 01, Karolinska Hospital, SE-171 76 Stockholm, Sweden.

SO Journal of general virology, (2003 Dec) 84 (Pt 12) 3443-52.

Journal code: 0077340. ISSN: 0022-1317.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200401

ED Entered STN: 20031217  
Last Updated on STN: 20040121  
Entered Medline: 20040120

AB The ability of murine pneumotropic virus (MPtV) major capsid protein VP1 to form **virus-like particles** (VLPs) was examined. MPtV-VLPs obtained were used to estimate the potential of MPtV to attach to different cells and to assess some characteristics of the MPtV cell receptor. Furthermore, to evaluate if MPtV-VLPs could potentially complement murine polyomavirus (MPyV) VP1 VLPs (MPyV-VLPs) as vectors for prime-boost **gene therapy**, the capability of MPtV-VLPs to serologically cross react with MPyV-VLPs and to transduce DNA into cells was examined. MPtV VP1 obtained in a recombinant baculovirus system formed MPtV-VLPs readily. MPtV-VLPs were shown by FACS analysis to bind to different cells, independent of MHC class I antigen expression. In addition, MPtV-VLPs did not cause haemagglutination of red blood cells and MPtV-VLP binding to cells was neuraminidase resistant but mostly trypsin and papain sensitive, indicating that the MPtV receptor lacks sialic acid components. When tested by ELISA and in vivo neutralization assays, MPtV-VLPs did not serologically cross react with MPyV-VLPs, suggesting that MPtV-VLPs and MPyV-VLPs could potentially be interchanged as carriers of DNA in repeated **gene therapy**. Finally, MPtV-VLPs were shown to transduce foreign DNA in vitro and in vivo. In conclusion, the data suggest that MPtV-VLPs, and possibly also MPtV, bind to several different cell types, that binding is neuraminidase resistant and that MPtV-VLPs should potentially be able to complement MPyV-VLPs for prime-boost gene transfer in vivo.

CT Check Tags: Human; Support, Non-U.S. Gov't  
Animals  
\*Antibodies, Viral: IM, immunology  
Capsid Proteins: IM, immunology  
\*Capsid Proteins: ME, metabolism  
Cell Line  
Cercopithecus aethiops  
Cross Reactions  
DNA-Binding Proteins: ME, metabolism  
Enzyme-Linked Immunosorbent Assay  
Guinea Pigs  
Hemagglutination  
Histocompatibility Antigens Class I: ME, metabolism  
Mice  
N-Acetylneurameric Acid  
Neuraminidase: PD, pharmacology  
Neutralization Tests  
Papain: PD, pharmacology  
Plasmids  
Polyomavirus: IM, immunology  
\*Polyomavirus: ME, metabolism  
Polyomavirus: UL, ultrastructure  
Protein Binding  
Receptors, Virus: CH, chemistry  
Receptors, Virus: DE, drug effects

RN Receptors, Virus: ME, metabolism  
Trypsin: PD, pharmacology  
RN 131-48-6 (N-Acetylneurameric Acid)  
CN 0 (Antibodies, Viral); 0 (Capsid Proteins); 0 (DNA-Binding Proteins); 0 (Histocompatibility Antigens Class I); 0 (Plasmids); 0 (Receptors, Virus); 0 (polyomavirus capsid protein VP1); EC 3.2.1.18 (Neuraminidase); EC 3.4.21.4 (Trypsin); EC 3.4.22.2 (Papain)

L7 ANSWER 3 OF 26 MEDLINE on STN  
AN 2003524218 MEDLINE  
DN PubMed ID: 14601522  
TI The use of **virus-like particles** for gene transfer.  
AU Petry Harald; Goldmann Claudia; Ast Oliver; Luke Wolfgang  
CS Berlex Biosciences, 2600 Hilltop Drive, PO Box 4099, Richmond, CA 94804-0099, USA.  
SO Current opinion in molecular therapeutics, (2003 Oct) 5 (5) 524-8. Ref: 53  
Journal code: 100891485. ISSN: 1464-8431.  
CY England: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
EM 200403  
ED Entered STN: 20031107  
Last Updated on STN: 20040331  
Entered Medline: 20040330  
AB A major challenge in the field of **gene therapy** is the development of new carrier/delivery systems that lack the disadvantages of current transfer systems. In the past, some time has been spent developing such modified or alternative vectors. A new candidate is represented by **virus-like particles** (VLPs). It has been shown that recombinant expression of the major structural proteins of many viruses leads to the formation of VLPs. Such VLPs exhibit morphology similar to the empty capsids of the virus from which they are derived. VLPs are non-infectious, have a similar tropism to the natural virus, and show comparable cellular uptake and intracellular trafficking. Since its discovery, VLP technology has gained importance in biomedical research. Although most investigations into VLP technology have dealt with vaccine development, some research groups have demonstrated that VLPs could also represent a useful **gene therapy** delivery system. This review will focus on studies performed with VLPs from members of the Papillomaviridae and Polyomaviridae families.  
CT Check Tags: Human  
Animals  
DNA, Viral: ME, metabolism  
\*Gene Therapy  
\*Gene Transfer Techniques  
Genetic Vectors: GE, genetics  
Genetic Vectors: IM, immunology

AN 2003510481 MEDLINE  
DN PubMed ID: 14557648  
TI Identification of a human papillomavirus type 16-specific epitope on the C-terminal arm of the major capsid protein L1.  
AU Carter Joseph J; Wipf Greg C; Benki Sarah F; Christensen Neil D; Galloway Denise A  
CS Program in Cancer Biology, Fred Hutchinson Cancer Research Center, Seattle, Washington 98109-1024, USA.. jcarter@fhcrc.org  
SO Journal of virology, (2003 Nov) 77 (21) 11625-32.  
Journal code: 0113724. ISSN: 0022-538X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200312  
ED Entered STN: 20031101  
Last Updated on STN: 20031219  
Entered Medline: 20031202

=> d 114 ab

L14 ANSWER 1 OF 1 MEDLINE on STN  
AB To characterize epitopes on human papillomavirus (HPV) virus-like particles (VLPs), a panel of mutated **HPV-16** VLPs was created. Each mutated VLP had residues substituted from HPV-31 or HPV-52 **L1** sequences to the **HPV-16 L1** backbone. Mutations were created on the HPV-31 and -52 **L1** proteins to determine if **HPV-16** type-specific recognition could be transferred. Correct folding of the mutated proteins was verified by resistance to trypsin digestion and by binding to one or more conformation-dependent monoclonal antibodies. Several of the antibodies tested were found to bind to regions already identified as being important for HPV VLP recognition (loops DE, EF, FG, and HI). Sequences at both ends of the long FG loop (amino acids 260 to 290) were required for both H16.V5 and H16.E70 reactivity. A new antibody-binding site was discovered on the C-terminal arm of **L1** between positions 427 and 445. Recognition of these residues by the H16.U4 antibody suggests that this region is surface exposed and supports a recently proposed molecular model of HPV VLPs.

=> d 122 2 all

L22 ANSWER 2 OF 3 MEDLINE on STN  
AN 97437475 MEDLINE  
DN PubMed ID: 9292008  
TI A monoclonal antibody against intact human papillomavirus type 16 capsids blocks the serological reactivity of most human sera.  
AU Wang Z; Christensen N; Schiller J T; Dillner J  
CS Microbiology and TumorbioLOGY Center, Karolinska Institute, Stockholm, Sweden.  
SO Journal of general virology, (1997 Sep) 78 ( Pt 9) 2209-15.  
Journal code: 0077340. ISSN: 0022-1317.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199710  
ED Entered STN: 19971013  
Last Updated on STN: 19971013  
Entered Medline: 19971001  
AB A type-specific and neutralizing mouse MAb (V5) against human papillomavirus (HPV) type 16 capsids was found to block the serological reactivity of human sera with the corresponding capsids. Out of 352 human serum samples tested for the presence of IgG against HPV-16, more than 75% of reactive sera were completely blocked by the **V5 antibody**. Type-specific MAbs against HPV-6, -18 and -33 were also found to block serological reactivity with capsids of the corresponding HPV types for the majority of reactive human sera. The results suggest that most antibodies in human sera that are reactive with intact HPV capsids recognize the same or closely related major antigenic determinant(s).  
CT Check Tags: Female; Human; Support, Non-U.S. Gov't  
Adolescent  
Adult  
Animals  
\*Antibodies, Monoclonal  
\*Antibodies, Viral  
Antibodies, Viral: BL, blood  
Binding, Competitive  
\*Capsid: IM, immunology

d 123 1 5 all

L23 ANSWER 1 OF 7 MEDLINE on STN  
AN 2004170965 MEDLINE  
DN PubMed ID: 15063127  
TI **HPV-16 L1** genes with inactivated negative RNA elements induce potent immune responses.  
AU Rollman Erik; Arnheim Lisen; Collier Brian; Oberg Daniel; Hall Hakan;  
Klingstrom Jonas; Dillner Joakim; Pastrana Diana V; Buck Chris B; Hinkula  
Jorma; Wahren Britta; Schwartz Stefan  
CS Department of Virology, Swedish Institute for Infectious Disease Control,  
Solna, Sweden.. erik.rollman@smi.ki.se  
SO Virology, (2004 Apr 25) 322 (1) 182-9.  
Journal code: 0110674. ISSN: 0042-6822.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200406  
ED Entered STN: 20040406  
Last Updated on STN: 20040602  
Entered Medline: 20040601  
AB Introduction of point mutations in the 5' end of the human papillomavirus type 16 (**HPV-16**) **L1** gene specifically inactivates negative regulatory RNA processing elements. DNA vaccination of C57Bl/6 mice with the **mutated L1** gene resulted in improved immunogenicity for both neutralizing antibodies as well as for broad cellular immune responses. Previous reports on the activation of **L1** by codon optimization may be explained by inactivation of the regulatory RNA elements. The modified **HPV-16 L1** DNA that induced anti-**HPV-16** immunity may be seen as a complementary approach to protein subunit immunization against papillomavirus.  
CT Check Tags: Support, Non-U.S. Gov't  
Animals  
Antibodies, Viral: BL, blood  
Antibodies, Viral: IM, immunology  
CD4-Positive T-Lymphocytes: IM, immunology  
CD8-Positive T-Lymphocytes: IM, immunology  
Cells, Cultured  
Disease Models, Animal  
Genes, Regulator  
Genes, Viral  
Lymphocyte Activation  
Mice  
Mice, Inbred C57BL  
Neutralization Tests  
Oncogene Proteins, Viral: GE, genetics  
\*Oncogene Proteins, Viral: IM, immunology  
Papillomavirus Infections: BL, blood  
\*Papillomavirus Infections: IM, immunology  
Papillomavirus Infections: PC, prevention & control  
Papillomavirus, Human: GE, genetics  
\*Papillomavirus, Human: IM, immunology  
Point Mutation  
Spleen: IM, immunology  
\*Vaccination  
Vaccines, DNA: AD, administration & dosage  
CN 0 (Antibodies, Viral); 0 (Oncogene Proteins, Viral); 0 (Vaccines, DNA); 0  
(oncogene viral capsid protein, **L1** human papillomavirus type 16)

L23 ANSWER 5 OF 7 MEDLINE on STN

AN 2003149974 MEDLINE  
DN PubMed ID: 12665934  
TI Construction and identification of the replication-deficient recombinant  
vaccinia virus co-expressing **HPV type 16**  
**L1** and **L2** proteins.  
AU Han Liqun; Ren Jiao; Liang Yu; Tian Houwen; Zhi Huijun; Luo Weifeng; Lu  
Zhenhua; Wei Lanlan; Ruan Li  
CS Institute of Virology, Chinese Academy of Preventive Medicine, Beijing  
100052, China.  
SO Zhonghua shi yan he lin chuang bing du xue za zhi = Zhonghua shiyan he  
linchuang bingduxue zazhi = Chinese journal of experimental and clinical  
virology, (2002 Sep) 16 (3) 256-60.  
Journal code: 9602873. ISSN: 1003-9279.  
CY China  
DT Journal; Article; (JOURNAL ARTICLE)  
LA Chinese  
FS Priority Journals  
EM 200311  
ED Entered STN: 20030401  
Last Updated on STN: 20031113  
Entered Medline: 20031112  
AB OBJECTIVE: To generate an HPV16 prophylactic vaccine candidate for  
cervical cancer. METHODS: HPV16 major capsid protein **L1** gene  
and minor capsid protein L2 gene were amplified using PCR. These genes were  
**mutated** by PCR site-directed mutagenesis for removal of sequence  
motifs (TTTTTNT) which would cause transcription termination when  
expressed from a vaccinia virus early promoter, then inserted into a  
vaccinia virus expression vector. A strain replication-deficient  
recombinant vaccinia virus containing the mutant sequences was obtained  
through a homologous recombination and identified. RESULTS: The  
nucleotide sequence remained the correct amino acid sequence of the  
**L1** and **L2** proteins after **mutated**. Full-length  
**L1** and **L2** proteins were generated in cells infected with the  
recombinant virus. The virus strain propagated at very low titer or could  
not reproduce in some kinds of cell derived from different human tissues.  
CONCLUSIONS: The authors have generated a strain replication-deficient  
recombinant vaccinia virus expressing HPV16 **L1** plus **L2** proteins  
as an HPV16 prophylactic vaccine candidate for cervical cancer.  
CT Check Tags: Female; Human; Support, Non-U.S. Gov't  
Capsid  
\*Capsid Proteins: GE, genetics  
Cell Line  
Cervix Neoplasms: VI, virology  
Cloning, Molecular  
English Abstract  
Gene Expression  
Genetic Vectors

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 1991:581030 CAPLUS  
DN 115:181030  
TI Type-specific and cross-reactive epitopes in human papillomavirus type 16 capsid proteins  
AU Beiss, Barbara K.; Heimer, Edgar; Felix, Arthur; Burk, Robert D.; Ritter, Diane B.; Mallon, Robert G.; Kadish, Anna S.  
CS Dep. Pathol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA  
SO Virology (1991), 184(1), 460-4  
CODEN: VIRLAX; ISSN: 0042-6822  
DT Journal  
LA English

=> d 125 2 ab

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN  
AB Rabbit polyclonal and mouse monoclonal antisera were raised to C terminal peptides from the genital human papillomavirus (**HPV**) 16 L1 and L2 open reading frames (ORFs). Anti-L1 and -L2 peptide sera recognized **HPV 16 L1** and L2 fusion proteins in Western blots and by immunopptn. In Western blot anal. of L1 proteins from different HPV types, antisera to the L1 peptide reacted only with **HPV 16**, thus identifying an **HPV 16** type-specific linear epitope. Anti-L2 peptide sera reacted with L2 fusion proteins from HPVs 6 and 16, but not from BPV, thus identifying a partially cross-reactive epitope in the **HPV 16** L2. Computer anal. of C terminal amino acid sequences of the L1 and L2 ORFs of multiple HPV types supported the Western blot findings. Despite the **HPV 16** type specificity found in Western blots, anti-L1 peptide sera identified nuclear antigen by immunocytochem. in cervical biopsies infected with **HPV 16**, as well as other genital HPV types. Anti-L2 peptide sera failed to recognize antigen in infected tissue.

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(FILE 'HOME' ENTERED AT 11:25:48 ON 12 AUG 2004)

FILE 'MEDLINE' ENTERED AT 11:26:06 ON 12 AUG 2004

L1        2479 S PAPILLOMA VIRUS  
L2        14951 S PAPILLOMAVIRUS  
L3        3154 S HPV TYPE 16 OR HPV-16  
L4        1758 S L1 AND L2  
L5        0 S L3 AND DELETED EPITOPE  
L6        0 S L3 AND DEVOID EPITOPE  
L7        41 S L3 AND MODIFIED  
L8        10 S L7 AND "L1"  
L9        4 S ITSE  
L10      0 S IMMUNODOMINANT TYPE SPECIFC EPITOPE  
L11      0 S DEVOID SPECIFIC EPITOPE  
L12      302 S L3 AND "L1"  
L13      0 S SPECIFC EPITOPE AND L12  
L14      1 S SPECIFIC EPITOPE AND L12  
L15      0 S EPITOPE DEPELETED  
L16      0 S EPITOPE DEPLETED  
L17      0 S DEPLETED EPITOP?  
L18      2 S DELETED EPITOP?  
L19      0 S L18 AND L2  
L20      0 S D9 ANTIBODY  
L21      0 S "D9" ANTIBODY  
L22      3 S "V5" ANTIBODY  
L23      7 S L12 AND MUTATED

FILE 'BIOSIS' ENTERED AT 11:44:34 ON 12 AUG 2004

L24      1 S L14

FILE 'CAPLUS' ENTERED AT 11:44:59 ON 12 AUG 2004

L25      2 S L14

FILE 'SCISEARCH' ENTERED AT 11:46:21 ON 12 AUG 2004

L26      1 S L14

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L15: Entry 3 of 4

File: DWPI

Mar 26, 2003

DERWENT-ACC-NO: 2001-281675

DERWENT-WEEK: 200327

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**TITLE:** Carrier for delivering substances to cells, useful in antitumor vaccines, comprises the major capsid protein of human papilloma virus modified to be nonimmunogenic

**INVENTOR:** ANTONSSON, P; DILLNER, J ; KRISTENSSON, K ; LANDO, P ; WALLEN-OHMAN, M ; WALLEN-OEHMAN, M

**PRIORITY-DATA:** 1999SE-0003534 (September 30, 1999)

  
**PATENT-FAMILY:**

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<input type="checkbox"/> HU 200202770 A2	December 28, 2002		000	C07K014/025
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ABSTRACTED-PUB-NO: WO 200123422A

BASIC-ABSTRACT:

NOVELTY - Carrier (A) for introducing a substance (I) into cells comprising the major capsid protein (L1) of human papilloma virus (HPV) that has been engineered to remove major type-specific epitopes that cause production of neutralizing antibodies is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) vaccines containing (A) as active ingredient;
- (2) polynucleotides (II) that encode (A); and
- (3) vaccines containing (II) as active ingredient;
- (4) the prevention or treatment of viral bacterial or parasitic infections by vaccination with (A).
- (5) the prevention or treatment of cancer by vaccination with (A).

ACTIVITY - Antitumor; antiviral; antibacterial; antiparasitic.

MECHANISM OF ACTION - Cytotoxic. Induction of a specific cytotoxic T cell response.

USE - (A), or the nucleic acid that encodes them, are used in vaccines for prevention or treatment of

- (i) viral, bacterial or parasitic infections, specifically infection by HPV; or
- (ii) benign or malignant consequences of HPV infections (specifically warts; laryngeal papillomatosis, and cancer of cervix, penis, vulva, vagina, anus or oropharynx).

ADVANTAGE - (A) does not induce production of neutralizing antibodies against itself, and may induce a response that is cross-reactive to several different HPV serotypes.

ABSTRACTED-PUB-NO: WO 200123422A

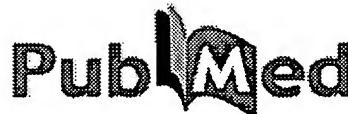
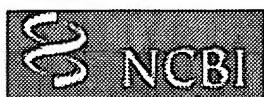
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